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CARCINOMA OF THE FEMALE BREAST: CONSERVATIVE AND RADICAL SURGERY

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"I have drawn the impression that in dealing with mammary cancer surgery meets with more peculiar difficulties and uncertainties than with almost any other form of the disease. The anatomical types are so numerous, the variations in clinical course so wide, the paths of dissemination so free and diverse, the difficulties of determining the actual conditions so complex, and the sacrifice of tissue so great, as to render impossible in a majority of cases a reasonably accurate adjustment of means to an end" (James Ewing, 1928).

In 1867 Charles Moore, of the Middlesex Hospital, introduced an extensive operation for the removal of a cancer of the breast. Since that time, through the labour of many surgeons, the operation of radical mastectomy has developed, until to-day Haagensen, after careful selection of cases, requires some five hours to ensure a complete dissection. The argument for radical surgery is simple: the only safety for the patient lies in the removal of every cancer cell from her body. By mechanical means the surgeon aims to remove what he cannot control, and there is no doubt that, with selection and extensive operation, survival rate has improved and local recurrence decreased. The advent of radiotherapy had a double effect on the management of "operable" cancer of the breast: first, it delayed the full study of Beatson's (1896) observations of the effect of the ovarian secretions on breast cancer; secondly, its use as a supplement to radical surgery, by improving the survival rate when the disease has extended beyond the breast into the regional glands, has tempted surgeons to operate when the disease is perhaps too far advanced.

It was in 1922, at St. Bartholomew's Hospital, that Mr. Geoffrey Keynes, at the suggestion of Professor George Gask, began an investigation into the treatment of recurrent cancer of the breast with radium. Impressed by the results obtained, he extended the method to include advanced primary cancer, and, later still, operable cancer, for he was gravely dissatisfied with the results of the radical operation. In a series of papers Keynes (1927, 1937a, 1937b) recorded his experience with conservative surgery and radium therapy. Primarily he hoped to mitigate or abolish the necessity for so drastic a form of treatment as the radical operation, which has a comparatively low absolute cure rate, and a definite morbidity in the form of oedema of the arm and limitation of movement at the shoulder-joint. As he gained experience Keynes maintained that, if the axillary lymph nodes are involved by growth, dissection of the axilla may be harmful, whilst if they do not appear to be invaded their dissection is unnecessary, provided radical irradiation is carried out in every case.

Anatomical investigation has shown no evidence for the centrifugal permeation of lymphatics by cancer cells. Keynes (1952) points out that Handley's work was done on pathological material taken from patients who had died of the disease, and that an abnormal state of affairs was taken as the basis for a system of treatment which was to be applied to all stages of the disease. It is only when the normal lymph channels are blocked that the cancer cell will seek out abnormal channels, such as those described by Handley. Some surgeons have been concerned lest, by dissecting the axilla, they open up pathways for the dissemination of the disease. It may, however, not be a question of opening up new pathways as much as the removal of normal pathways, leaving only abnormal ones for dissemination.

Death from cancer of the breast is almost always due to metastases transported by lymphatic or venous embolism. The recent work of Richard Handley (Handley and Thackray, 1947; Handley, 1952) has shown that, as well as the axillary glands, those along the internal mammary vessels are frequently invaded and can be regarded as immediate regional lymph nodes draining the breast. The internal mammary glands form one of the routes for intrathoracic and more distant spread, and lie outside the scope of the classical radical operation. In order to be successful, treatment must be carried out before the onset of distant metastases. Even in clinical stage I distant spread has already taken place in about 20% to 30% of patients, but once the axilla is invaded the incidence is much higher. In either stage,

if the addition of radiotherapy to radical surgery improves the results, it must be because irradiation has destroyed (or confined) cancer cells still remaining within the treated tissue. It can be argued that, in clinical stage I, radical surgery is too radical and that the chance of peripheral but still regional lymphatic spread can be met by full post-operative irradiation.

In stage II radical surgery can deal only with about one-third of cases successfully, and in the remainder the disease is already beyond the reach of the surgeon's knife. Keynes maintained that in these cases simple removal of the tumour, which may mean simple mastectomy, with simple excision of accessible lymph nodes and no disturbance of the axilla by dissection, together with full post-operative irradiation, would achieve the same result as radical mastectomy and irradiation without the morbidity of the larger operation. Indeed, if radical mastectomy exposes the patient to the risk of spread by abnormal channels the results of conservative surgery and irradiation may be better than those of more radical surgery. Surgery and radiotherapy balance each other in the eradication of cancer cells within a similar volume of tissue, and the scope of surgery can be decreased provided the radiotherapy is thorough. Actually the scope of radiotherapy is greater, for it can include the whole skin area from clavicle to costal margin and sternum to back. It can embrace the lymph nodes in the internal mammary region, the neck, the axilla, and the pathways and tissue planes in between. It can exert its full action only if anatomy and physiology have not been too seriously interfered with, and in skilled hands it can do this without risk of immediate morbidity.

Ewing pointed out many years ago that the radical operation was, on the one hand, performed too often on comparatively innocent growths, such as encapsulated adenocarcinoma, and localized duct cancers which may be ablated by simple mastectomy; and, on the other hand, on highly malignant forms of the disease which are invariably fatal. The good result in the first type of case is ascribed falsely to sacrifice of tissue, whilst in the other type of case the extreme limits of tissue removal will not save the patient.

The Present Investigation

The unique nature of the material available in the records of St. Bartholomew's Hospital for 1930 to 1939 inclusive suggested that a retrospective inquiry might be of real value in answering some of the problems of mammary cancer. During this decade a large number of cases were treated, chiefly by Keynes but also by the surgical professorial unit, by a method which was at that time considered highly unorthodox. In view of the continued dispute about the merits of radical and more conservative treatment there seemed to us to be a real advantage in comparing the results of these different methods of treatment during the same period of time, when conditions were more or less uniform. It must be recognized, of course, that certain problems may be answered only by a planned research, such as one in which alternate cases are allocated to different treatment groups. Nevertheless, it would hardly be justifiable to do this unless one had substantial evidence, such as we believe is provided by the present material, that the ultimate results are much the same for different methods of treatment.

Objects and Scope of Inquiry

We set out to analyse the results of treatment of all the new cases of primary carcinoma of the female breast seen at St. Bartholomew's Hospital during the years 1930–9 inclusive, but excluding cases sent on for radiotherapy after operation elsewhere. The main objects of the analysis were: (1) To endeavour to assess the relative merits of radical surgery and conservative surgery, together with radiotherapy in the treatment of cancer of the female breast. (2) To find out what part radiotherapy plays in the treatment, its effect on local recurrence rate, and its effects on survival. (3) To determine the morbidity of treatment, with special reference to oedema of the arm and the possible influence of radiotherapy. (4) To decide whether the radical operation justifies itself in terms of survival and morbidity. (5) Finally, if different methods of treatment have their special indications, to try to find out how the doctor may decide the best method for each particular patient.

From the total number of cases registered in the follow-up department, 182 patients from previous years with recurrent tumours were excluded, as were 102 cases operated on at other hospitals. In addition there were 60 cases for which the records were incomplete, and it was impossible to determine whether or not they should have been included. In all, 1,044 cases were available for analysis.

St. Bartholomew's Hospital, in common with other London teaching hospitals, draws its patients from a wide and indeterminate area. The existence of a large radiotherapy centre has probably been the reason for the greater number of advanced cases than is seen in most series, but otherwise there is no reason to suspect any particular selection. Once referred to the hospital, all malignant cases were registered in the follow-up department.

Follow-up and Method of Inquiry

Of the 1,044 cases all but 30 (2.9%) were followed up, either by frequent examination at the out-patient department or by postal inquiry, until May, 1951, or the time of their death. This has enabled ten-year survival rates to be calculated for the whole series, and fifteen-year rates for those registered during the six years 1930–5.

Apart from registration in the follow-up department no uniform methods of recording were used, and the only material available for study has been the routine clinical notes taken by students, house-surgeons, registrars, and consultant staff. All the records were scrutinized by two of us (I. G. W. and R. S. M.) during a period of five months in 1952, the most important details being transcribed on to special forms from which Hollerith cards were punched.

Clinical Staging.—Many of the cases had been staged at the time of first diagnosis, but as uniform methods had not always been used all were staged afresh from such information on the clinical condition as was available. The method used was a modification of the so-called "Manchester" system.

Stage I.—The tumour is freely mobile on muscle or chest wall. Ulceration or involvement of the skin must be no larger than the primary tumour and directly in continuity with it.

Stage II.—There are now palpable lymph nodes, considered to be metastases, in the axilla of the same side.

Stage III.—The primary growth is larger, and is now fixed to muscle but not to chest wall. Skin involvement can be wide of the primary tumour but is still over the breast. Axillary glands, if infected, must be mobile.

Stage IV.—The growth has extended beyond the breast and immediate regional lymphatic glands. Fixation of axillary glands or fixation of the primary to the chest wall places the tumour in stage IV.

The distribution by clinical stages for the whole series is shown in Table I.

TABLE I

	Clinical Stages				Unstaged	Total
	I	II	III	IV		
No. of cases	339	302	286	106	11	1,044
% ..	32·5	28·9	27·4	10·2	1·1	

General Features of the Series

Age.—The age distribution of the whole series was as follows:

Years:	0–	25–	35–	45–	55–	65–	75–	Not Stated	Total
Number ..	3	37	190	317	298	159	38	2	1,044
% ..	0·3	3·5	18·2	30·4	28·5	15·2	3·6	0·2	

This follows the familiar pattern with nearly 60% of cases falling into the group 45–64. Over the age of 65 there were perhaps fewer cases than appear in most comparable series—for example, 18.9% compared with 29.0% given by Harnett (1948). The proportion of single women was 21%, and this agrees with other published series. There were three cases of lactation carcinoma, and in four cases

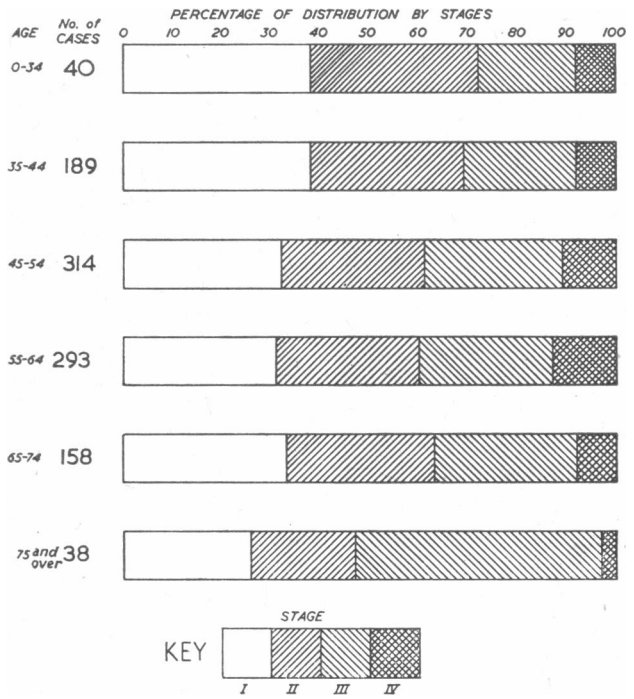

FIG. 1.—Distribution of clinical stages according to age. Eleven cases with stage unknown and one other case with age unknown are excluded.

the disease was diagnosed and treated during pregnancy. Fig. 1 shows the distribution of clinical stages for the different age groups. Of women aged less than 45 about 70% had tumours which were in clinical stages I and II, whereas at all ages from 45 to 75 the corresponding proportion was about 60%. There were only 38 women aged 75 or more, and half of these were in stages I and II.

Site of Tumour.—The site of the tumour in the breast was recorded in all but 26 cases, although the quadrant was not always specified. Fig. 2 shows the percentages occurring in the four quadrants and also of those simply recorded as "upper," "lower," "inner," or "outer." In 8% of cases the tumour was described as central, and 12% filled the whole breast. Exact comparison with other series is made difficult by the absence of precise definitions. For the purposes of later analysis all inner and all outer tumours have been grouped together, other sites being, for this purpose, ignored. Of the 502 outer-half tumours, 37% fall into stage I and 35% into stage II. The corresponding figures for the 182 inner-half tumours are 46% and 29%. Simultaneous bilateral tumours were recorded in eight cases, giving a slightly lower proportion than has been noted by other observers. For the rest of the series the excess of left-sided over right-sided tumours was 11%, a figure that agrees closely with those cited by Nohrman (1949). Among these were 37 (4%) in which the other breast was, either previously or subsequently, the site of a carcinoma; but there is, of course, a possibility of confusion between some of these cases and the true simultaneous tumours.

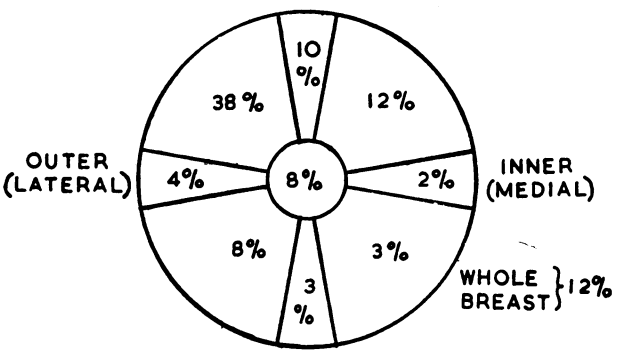

FIG. 2.—Distribution of tumours by site. The narrow sectors indicate the proportions of tumours recorded simply as "upper," "lower," etc. The percentages are calculated from the whole series less the 8 cases with bilateral tumours and the 26 for which no exact site was recorded.

Length of History.—Were it possible to obtain accurate information of the time when the lump in the breast first appeared it might be possible to calculate some sort of index of growth rate, or essential malignancy for each tumour. But, in the nature of things, such information is unobtainable, and all we can give is the length of time for which the patient can remember symptoms. This length of history is naturally correlated with the clinical staging, as is shown in Table II, but not to such an extent that all difference in

TABLE II.—*Clinical Staging and Length of History*

Length of History (To Nearest Month)	No. of Cases	Distribution by Stages I	II	III	IV
1 month	117	40%	41%	13%	6%
2 months	122	40%	34%	18%	7%
3 ,, ...	107	37%	26%	24%	12%
4–6 months	222	39%	28%	25%	8%
7–11 ,, ...	230	23%	29%	33%	15%
1 year–	118	25%	26%	40%	9%
2 years–	93	31%	21%	40%	8%

This table excludes 33 cases with unknown length of history and two other unstaged cases.

staging can be explained in this way. For example, 19% of the 117 patients with only one month's history of symptoms were in stages III or IV by the time that they were seen, whilst of the 93 women who claimed more than two years' history no less than 31% were still in stage I.

Pathological Grading and Staging.—Histological reports were usually available, but it was clear that any attempt to grade the tumours from the reports alone in the manner suggested by Bloom (1950) would not be justified. It was not found practicable to study the original sections. It was, however, recorded whether or not the axillary glands had been invaded, and this will be referred to as the pathological staging. Pathological reports were available in 448 of the 505 cases in which the axilla was dissected, and Table III

TABLE III.—*Clinical Staging and Gland Involvement*

Stage	No. of Cases with Axillary Dissection	No. of Cases with Histological Reports	Percentage Reported as Having Glands not Involved
I	184	164	71%
II	202	180	23%
III	103	93	17%
IV	13	11	—

This table includes all cases subject to radical or modified radical surgery, other than three unstaged cases.

shows the results according to the clinical staging. It will be seen that for stage I the clinical assessment was upheld by the pathology report in 71% of cases, whilst in the remaining 29% the clinician had been unable to detect an involvement which was later proved to be present. In stage II, on the other hand, there were 23% of cases in which the clinician reported gland involvement which the pathologist was unable to confirm. It is perhaps interesting that whereas, as has been shown, there is an appreciable association between length of history and clinical staging, there is no such clear association between length of history and gland involvement. This may be seen from the following analysis. If we take the 428 cases in clinical stages I, II, and III (omitting the few for whom the length of history was not given), the following percentages are the proportions of cases in each stage *with a length of history of six months or more:* Stage I, 43% (161); Stage II, 54% (177); Stage III, 64% (90). If these same cases are now divided according to the histological reports we have: Glands free, 51% (170); involved, 52% (258), the figures in parentheses being the numbers of cases on which the percentages are based.

Methods of Treatment

The methods of treatment used in this series are shown in Table IV; there were three main surgical treatment groups: simple surgery, radical surgery, and modified radical surgery. Each of these three groups is further subdivided into surgery alone, surgery with *x* rays, and surgery with radium. A few of the cases treated initially by simple surgery had more extensive operations at a later date, but the figures in the Table refer only to the primary treatment and not to any subsequent operations or irradiation.

TABLE IV.—*Methods of Initial Treatment for the Whole Series*

	With *X* Rays	With Radium	Without Irradiation	Total
Simple surgery	70	101	58	229
Radical ,, ...	147	7	184	338
Modified radical surgery ..	51	70	46	167
Without surgery	114	149	47*	310
Total ..	382	327†	335	1,044

* Untreated cases. † Includes two cases treated with radium and *x* rays.

Simple Surgery.—This group comprises 229 cases, 58 being treated by operation alone, 70 by simple surgery and *x* rays, and 101 by simple surgery and radium. The operation was confined to simple excision of the tumour in 127 cases and the remaining 102 had a simple mastectomy. Two-thirds of the cases were under the care of Keynes or the surgical professorial unit. In the earlier years Keynes tended to do local excision of the tumour, but the occasional occurrence of carcinoma elsewhere in the breast led to his adoption of simple mastectomy in most cases. Ten of the 127 simple excision cases had more radical surgical treatment at a later date; these include one modified radical operation four months after local excision and *x* rays, and three modified radical and six radical mastectomies from one to thirteen years after simple excision and radium treatment. Even after excluding these ten secondary operations for persistent or recurrent disease it should be noted that more than half the cases in the simple surgery group were treated by the minimum of surgery.

Radical Surgery.—Radical mastectomy with or without irradiation was performed as the initial method of treatment in 338 cases—that is, in 32% of the whole series. Fig. 3 shows that the proportion remained fairly steady throughout the whole 10 years. A study of the case records of those treated by radical surgery and knowledge of the practice of individual surgeons indicate such variations in surgical technique as one would expect among different operators. (The operations were done by 12 members of the consultant staff and their chief assistants and also by the professorial staff.)

Modified Radical Surgery.—This is the descriptive title used for simple mastectomy and axillary clearance without removal of the pectoral muscles. A special group of 70 cases treated by modified radical mastectomy by the surgical professorial unit formed a research series which has been reported by Professor Sir James Paterson Ross (1938). This

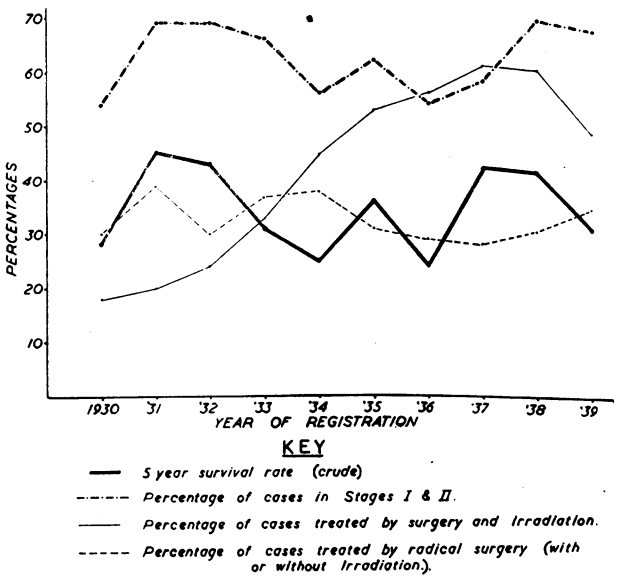

FIG. 3.—Crude five-year survival rates for cases registered each year, compared with percentage of cases in clinical stages I and II.

was an almost consecutive series of cases in which mastectomy followed radium treatment after an interval of three months in 50 cases and of six months in the remainder, and the operation was done with the object of providing material evidence of the effects of irradiation rather than as a method of treatment *per se*. This series is too small to permit any definite conclusions about the value of this form of combined treatment. The reasons for performing this operation were not often given in the records of the remaining cases, but sometimes it was done in elderly or less fit patients in whom the radical operation was considered too severe. It is an operation which provides fuller pathological data than simple mastectomy, but it is doubtful whether there is any direct therapeutic advantage.

Irradiation

Radium treatment alone was used initially in 149 cases, but subsequent simple mastectomy was done in 13; radical mastectomy in 7, and modified radical mastectomy in 5. About a quarter of those treated by radium alone were in stage I, but as the diagnosis was not always confirmed by biopsy one must be cautious in assessing the results for radium treatment alone.

Simple surgery and radium were combined in the treatment of almost half the cases dealt with by limited surgery. The technique of radium therapy was that described by Keynes (1929, 1932), and it will not be further discussed here. Radium was combined with radical surgery in seven cases, all of which were treated in the earlier part of the decade under review, when *x*-ray methods were still being developed.

X-ray treatment alone was reserved chiefly for advanced cases, and only 6% of this group was in stage I. Rarely was the diagnosis confirmed by biopsy. *X* rays and simple surgery were used less often than the combination of radium and simple surgery, although, in the light of experience, the former method gradually became more popular.

Radical surgery and *x*-ray therapy, generally post-operative, was used in almost half the radical mastectomy cases. Dosage was in the region of 4,000 r minimum, during a period of four weeks, directed to the chest wall, axilla, and

supraclavicular regions. In 15 cases the treatment was given pre-operatively, the usual reasons being either a large growth or advanced disease. With so many different surgeons at work and in the absence of any well-defined criteria for *x*-ray treatment, it is not possible to give any clear indication of how cases were selected for irradiation. Towards the end of the period under review some surgeons were tending to refer all patients for post-operative radiotherapy, but in general those irradiated included a higher proportion of less favourable cases. Fig. 3 shows how the combination of surgery and irradiation became increasingly popular, the proportion thus treated being 18% in 1930 and 60% in 1938, although it fell to 48% in 1939.

Untreated Cases.—Of the 47 untreated cases 14 were in stage III and the remainder in stage IV. Only two patients in the whole series refused all treatment.

Assessment of the Results of Treatment

Discussion has raged for many years regarding what is the most appropriate way to measure the results of treatment of cancer of the breast. A whole battery of statistical and actuarial techniques has been introduced, but in spite of this there is still no general agreement on the fundamental question of how long, if at all, life is prolonged by any form of treatment. Greenwood (a pioneer in this field) asserted (1926): "The expectation of life of a woman with untreated cancer of the breast is 3.25 years, the expectation of life of a woman operated on under 'average' conditions is 5.74 years and of a woman operated on under the best conditions is 12.93 years." His analysis may seem somewhat naive to our present way of thinking. At the other extreme we have Park and Lees (1951): "It has not been proved that the survival rate of cancer of the breast using the five-year survival rate as an index is affected by treatment at all."

This is not the place to discuss the statistical problems involved, for we are concerned in this paper only with the *relative* results of different forms of treatment: in choosing the statistical method most appropriate to our purpose our chief requirements are: (1) that the method chosen should be simple to use and understand; (2) that it should be reasonably sensitive; and (3) that it should allow for any gross bias introduced by selection between the groups.

The method we have adopted is to express our results in terms of five- and ten-year survival rates calculated separately for the different stages and adjusted by Berkson's (1942) method to allow for variations in the age distribution. Fifteen-year survival rates have also been calculated for the 600 cases registered from 1930 to 1935.

Recent observers are agreed that staging, whether assessed clinically or pathologically, is the most important single factor in prognosis. This is clearly demonstrated by Fig. 3, in which are plotted: (i) the crude five-year survival rates for all cases registered in each of the years 1930–9, and (ii) the percentages of stages I and II cases among each year's registrations. It will be seen that the two graphs have an almost identical pattern. (The other graphs plotted on this diagram have been referred to already.) The survival rates for the different stages are so different that little or no useful information can be gained from a study of figures in which no distinction is made between them. Even methods of standardization, such as that recommended by Park and Lees (1951), are open to serious disadvantages.

In using time of survival as an index of the success of treatment it is clear that no satisfactory comparison can be made without taking age into consideration. For example, in 1931 the expectation of life of a woman of 40 was about 32 years compared with only 10 years for one of 70. This difficulty is particularly important in a disease like carcinoma of the breast, where there is a relatively high survival rate even at 10 years. One solution of the problem is to confine analysis to those actually dying of cancer; if all patients lived and died under the care of the hospital where they were first treated this might be the ideal solution, but in practice it leads to difficulties. We have preferred, therefore, to use the method first proposed by Berkson and now adopted by W.H.O. (1950)* for the purposes of international comparisons.

For any group of people of known ages it is possible to calculate the number who may be expected to be alive after a given number of years, assuming that they are subject to the normal mortality experience of the whole country as expressed on the Registrar-General's Life Tables. We can therefore define the crude and adjusted rates as follows:

$$\text{Crude rate} = \frac{\text{No. alive and traced after } n \text{ years}}{\text{No. originally registered}} \times 100$$

$$\text{Adjusted rate}^* = \frac{\text{No. alive and traced after } n \text{ years}}{\text{Expected No. alive after } n \text{ years}} \times 100$$

It will be seen that no allowance is made for the possible survival of any of the untraced cases.

The chief advantage of this method is that it is entirely objective, but one disadvantage is that it is effective only for groups of such a size as to even out chance fluctuations in the number of deaths due to intercurrent disease. The effect of the adjustment is illustrated by the following figures, showing the crude and adjusted rates for two age groups:

		10-year Survival Rates	
		Crude	Adjusted
Stage I cases	Ages 0–44	45%	48%
	,, 65–	22%	49%

When comparing treatment groups there was not as much difference as this between the crude and adjusted rates, for there were no very great differences in the age distributions of the groups under consideration. Nevertheless the adjustment is certainly worth making when ten- or fifteen-year rates are being used.

Another problem that has to be solved is that of defining the groups for which survival rates shall be calculated. There are so many factors, such as age, stage, and site, as well as variations in surgical and non-surgical treatment, that it would be impossible from a series of the size available to a single hospital to split up the figures in such a way as to enable the effect of all these factors to be sorted out. In order to get any results at all a fairly drastic grouping has to be accepted—the more so since, as has been said, it has been felt necessary to give all results separately for the four clinical stages. But to ensure that no important effect has been masked by such grouping, we have in most instances examined the figures in greater detail than can be shown here.

In the following analysis no mention is made of the statistical significance of the results. In a retrospective survey of this kind formal tests of significance are often most misleading. Little is known of what selective factors may have been at work, and the very methods of grouping introduce a highly subjective element into the calculations; it is often possible to change a "significant" into a "not significant" result merely by making an arbitrary change in the classification. All we shall do is to present the survival rates we have calculated and draw such tentative conclusions from them as we feel able.

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* The formula given by the W.H.O. report is as follows:

$$\text{Corrected survival rate} = \frac{1}{p} \times (\text{crude survival rate})$$

where p is the probability of not dying within a comparable period from any cause other than cancer of the site in question, in a population having the same age distribution as the patients comprising the group. The report points out that for most sites p does not differ appreciably from the probability of not dying from any cause, and although the female breast might be regarded as one of the sites where the distinction *should* be drawn, we have not felt it necessary when using the adjustment only for internal comparisons. Our definition is equivalent to the W.H.O. formula, but defining p as the probability of not dying from any cause.

The W.H.O. report does not recommend a method of calculating p, and there is some variation of practice in the matter. To calculate the expected number of survivors we have used the values for women of ${}_5p_x$, ${}_{10}p_x$, and ${}_{15}p_x$ derived from English Life Table No. 10 (1930–2) (and kindly supplied by the General Register Office). For our purposes it has been sufficiently accurate to use ten-year age groups for the calculations.

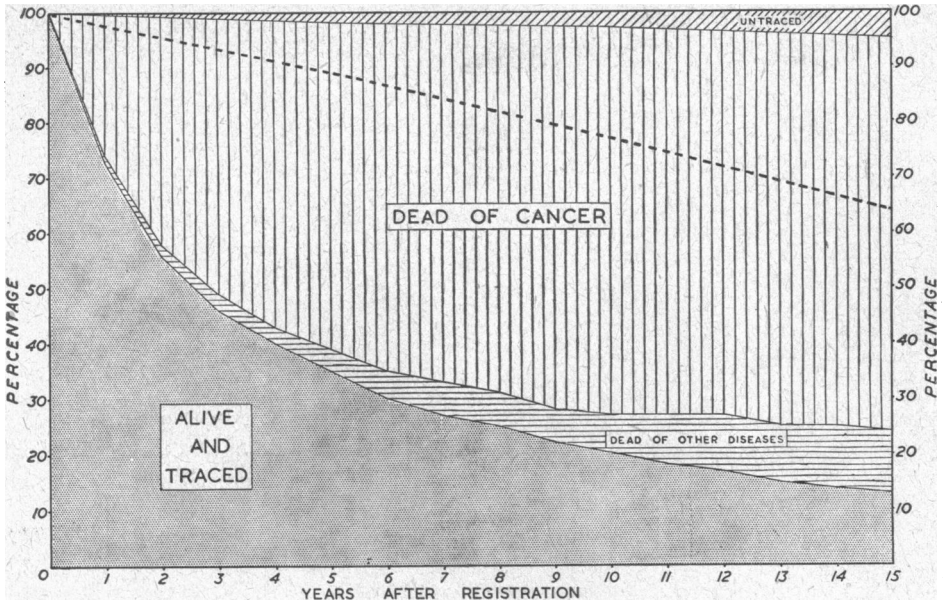

FIG. 4.—Percentages dead and alive based on whole series (1–15 years). (The dotted line indicates the expected survival of a normal group with similar age distribution based on Life Table for 1931.)

Although it is not our object to discuss the overall results of the series, it may be of interest to give them in the form of Fig. 4; this shows the crude survival rates for the whole series (including untreated cases) from one to ten years and for the 600 cases registered between 1930 and 1935 from 10 to 15 years. The numbers recorded as dying of recurrent disease and those untraced are also shown.

Results of Treatment

In presenting results we have compared the survival rates for the different types of surgical treatment—that is, simple, radical, and modified radical surgery—and also those for surgery alone and surgery with irradiation. The number of cases in each of the various subgroups shown in Table IV is generally too small for any comparison of the results obtained, with the possible exception of radical mastectomy. In Fig. 5 the results are shown for five main treatment groups, the various subgroups being ignored. The simple, radical, and modified radical surgery groups include all cases treated by these methods regardless of whether irradiation was also given. The last two groups—surgery alone and surgery with irradiation—include all surgical cases irrespective of the type of operation done. Full details of the various subgroups are shown in Table V to supplement the information given in Fig. 5.

Simple Surgery and Radical Surgery.—Fig. 5 shows that at the five-year follow-up the adjusted survival rates in stage I are slightly in favour of simple surgery, but that this trend is reversed at ten years. Modified radical surgery shows a lower five-year and a higher ten-year survival rate, but there are only 37 cases in this group. In stage II cases the survival rates are almost identical for the three types of surgery.

In assessing these results it should be remembered that the simple surgery group includes 127 cases treated by simple excision of the tumour. Only 10 of these subsequently had a more extensive operation, and the other 117 cases were therefore treated by an operation which most surgeons would regard as quite inadequate. The fifteen-year adjusted survival rates (calculated from the 600 cases registered between 1930 and 1935 inclusive) were 42% for simple surgery, 42% for radical surgery, and 37% for modified radical surgery, the crude survival rates being 28%, 27%, and 26%. We must conclude from these figures that the results for simple surgery are as good as those for radical surgery.

Surgery Alone and Surgery with Irradiation.—Radiotherapeutic technique was developing during the decade in question, and it may be that the selection of cases was not

TABLE V.—*Adjusted and Crude Survival Rates for Stages I–III According to Method of Treatment*

	All Cases Stages I–III	Stage I			Stage II			Stage III		
		Total Cases	Survival Rates Adjusted and Crude (%)		Total Cases	Survival Rates Adjusted and Crude (%)		Total Cases	Survival Rates Adjusted and Crude (%)	
			5-year	10-year		5-year	10-year		5-year	10-year
All treated cases	913	339	72 (65)	51 (40)	302	39 (35)	26 (20)	272	12 (11)	4 (3)
Simple surgery:	216	110	76 (69)	47 (37)	45	41 (36)	31 (22)	61	15 (13)	6 (5)
Without irradiation	55	30	86 (77)	43 (33)	7	—	—	18	—	—
With *x* rays	63	20	—	—	9	—	—	34	10 (9)	4 (3)
„ radium	98	60	73 (67)	49 (40)	29	39 (35)	27 (21)	9	—	—
Radical surgery:	329	147	72 (65)	52 (41)	122	41 (38)	26 (22)	60	9 (8)	4 (3)
Without irradiation	180	88	71 (62)	50 (38)	63	46 (43)	25 (21)	29	11 (10)	4 (3)
With *x* rays or radium	149	59	73 (68)	55 (46)	59	34 (32)	28 (24)	31	7 (6)	4 (3)
Modified radical surgery:	160	37	58 (54)	55 (46)	80	42 (38)	25 (19)	43	20 (19)	8 (7)
Without irradiation	45	13	—	—	26	31 (27)	16 (12)	6	—	—
With *x* rays	48	3	—	—	24	—	—	21	—	—
„ radium	67	21	—	—	30	44 (40)	34 (27)	16	—	—
All surgery without irradiation	280	131	73 (65)	48 (37)	96	43 (39)	24 (19)	53	20 (17)	8 (6)
„ „ with „	425	163	71 (65)	53 (43)	151	40 (36)	28 (23)	111	12 (11)	5 (5)
Irradiation alone:	208	45	75 (64)	50 (36)	55	31 (27)	22 (16)	108	9 (7)	1 (1)
X rays	71	7	—	—	6	—	—	58	0 (0)	0 (0)
Radium	137	38	75 (66)	56 (42)	49	30 (27)	19 (14)	50	19 (16)	3 (2)

(*a*) The following cases are omitted from this table: 106 cases in Stage IV, only one of whom survived 5 years; 14 untreated cases in Stage III, none of whom survived 5 years; 11 unstaged cases.
(*b*) Survival rates for subgroups containing fewer than 25 cases are not shown.
(*c*) The crude survival rates are shown in parentheses.

such as to allow the benefits of radiotherapy to be clearly demonstrated. Fig. 5 shows that the five-year survival rates in stages I and II were practically the same for all surgery alone and all surgery with irradiation. The ten-year survival rates were, however, slightly higher for surgery with irradiation in both stages. Fuller details of the subgroups are given in Table V, where it will be seen that radical mastectomy with irradiation gave slightly better survival rates than radical surgery alone in stage I at five- and ten-year follow-up. The results were also better at ten years in stage II. However, in both cases the numbers were small, and it is impossible to draw firm conclusions.

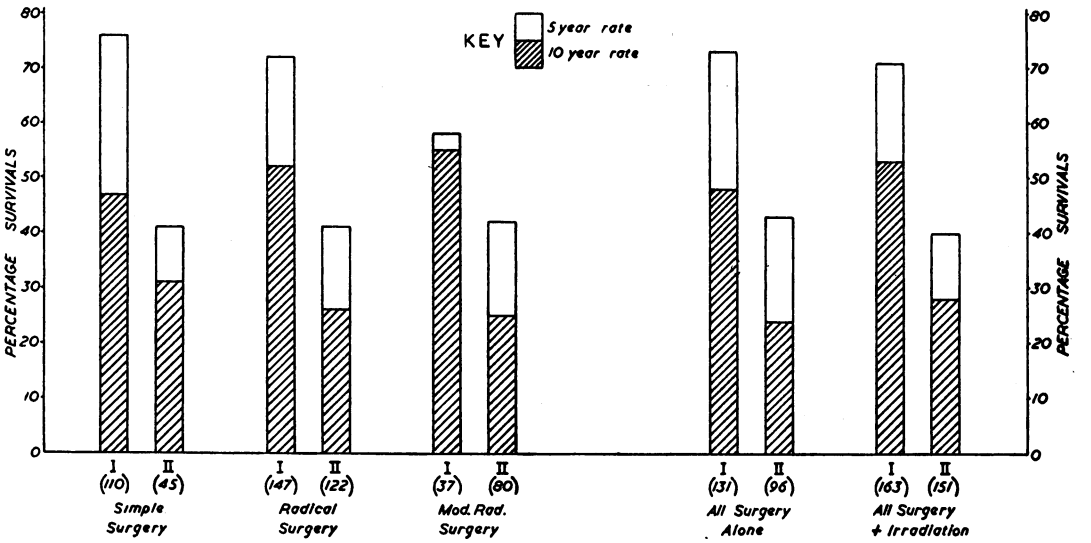

FIG. 5.—Adjusted five-year and 10-year survival rates for surgical cases (stages I and II only). The figures in parentheses are the numbers of cases from which the survival rates are calculated.

Value of Clinical and Pathological Staging

It is commonly assumed that pathological staging is superior to clinical staging in the assessment of prognosis, but it would be better to say that the methods are complementary. In those cases in which the axilla is not dissected the staging must necessarily be clinical, and even where the axilla is dissected the pathological examination of the axillary glands is, as Handley (1952) has shown, by no means the last word. The margin of error in clinical staging has already been referred to; but, despite this, there seems reason to believe that clinical assessment of the axilla may offer a more accurate clue to prognosis than might be expected. Table VI shows the five- and ten-year survival rates for 447 cases, treated by radical or modified radical mastectomy, in which a pathological report on the axillary glands was available. The cases in clinical stages I and II are subdivided into those with glands free and those with glands involved. The second and third columns of figures in this table represent, therefore, those cases in which the clinician was wrong in his assessment of the axilla.

TABLE VI.—*Gland Involvement: Five- and Ten-year Adjusted Survival Rates for Cases in Stages I–III after Radical or Modified Radical Surgery.*

	Stage I		Stage II		Stage III
	Glands Free	Glands Involved	Glands Free	Glands Involved	All Cases
No. of cases	117	47	42	138	103
5-year survival rate	78%	52%	51%	37%	14%
10- ,, ,, ,,	67%	25%	29%	22%	5%

There are not enough cases in Stage III with glands free to enable separate figures to be given (see Table III), but overall rates are included for purposes of comparison.

The lower five-year and ten-year survival rate in stage I with glands involved as compared with stage I cases with glands free is readily understandable. It is, however, less easy to comprehend why stage II with glands free should show the same survival rate as stage I with glands involved. This might be regarded as just a strange anomaly in our figures, but a similar state of affairs is indicated in a table of Smithers (1952), on which no comment is offered in the text.

The practical importance of this finding would seem to be that, in those cases in which the clinician believes the axillary glands to be involved, the prognosis may be much the same, regardless of whether the diagnosis is confirmed pathologically. The high incidence of reactive hyperplasia in the axillary glands of breast carcinoma cases is, of course, well recognized by pathologists. The cause of the reactive hyperplasia which produces the enlarged but cancer-free glands is not known, but Professor Hadfield (1952, personal communication) believes that it may be related to the microscopic foci of necrosis throughout the tumour. Whatever the explanation of this interesting finding may be it does seem to be a matter worthy of fuller attention and investigation, for its relationship to a more serious prognosis is not explicable in terms of orthodox pathology.

Apropos of clinical staging, it is perhaps important to recognize that a clinician is more likely to detect a just palpable axillary gland and to examine the patient more carefully if the primary tumour is a large one. It is likely that this factor—that is, the size of the tumour—explains some of the difference in prognosis in these cases, but it will not adequately explain the similar prognosis for stage I cases with glands involved and stage II cases with glands free.

Site of Tumour and Prognosis

Several published reports (Perry, 1925; Truscott, 1947; Smithers, 1952) have recorded lower, but not significantly lower, five-year survival rates for growths in the medial half of the breast.

For our series, as shown in Table VII, the five-, ten-, and fifteen-year survival rates in stage I were much the same for tumours in medial and lateral halves of the breast. In stage II cases, however, the survival rate was slightly lower for tumours in the medial half of the breast; but this is only what might be expected, since a medially situated tumour with axillary glands palpable is likely to be at a

TABLE VII.—*Lateral and Medial Tumours: Five-, Ten-, and Fifteen-year Adjusted Survival Rates for Surgical Cases in Stages I and II.*

	Stage I		Stage II	
	Lateral	Medial	Lateral	Medial
Whole series:				
No. of cases	159	71	136	41
5-year survival rate ..	73%	70%	47%	38%
10- ,, ,, ..	52%	53%	29%	25%
1930–5 series: ,, ..				
No. of cases	94	39	82	19
15-year survival rate ..	42%	43%	28%	(15%)

more advanced stage of its development than a laterally situated tumour with palpable glands. Handley (1952) has shown that the internal mammary lymph nodes are invaded in 60% of cases with medial tumours, and in only 19% with lateral tumours, and on this evidence one would anticipate a worse prognosis for those patients with medially situated tumours.

Despite the greater ease with which the medial growth may reach the mediastinum our own figures would suggest that, in the absence of palpable axillary glands, prognosis is no worse for a tumour in the medial half than for one in the lateral half, and this is a point of some importance to the clinician faced with the daily problems of breast carcinoma.

Length of History and Prognosis

It may be asked whether we can demonstrate from our figures that delay in seeking advice worsens the prognosis. This is a most difficult question and one that obviously cannot be answered directly. In so far as longer history is associated, as we have shown, with tumours of a more advanced stage, which undoubtedly have a worse prognosis, then the answer is clear. A more detailed analysis, for which there is not space here, seems to show that for tumours of a given stage (as assessed both clinically and pathologically) the ones with a long history do no worse or better than those with a short history.

Mortality and Morbidity of Treatment

Mortality.—Four out of 338 patients died after radical mastectomy, a mortality of 1.2%. Three of these four deaths were due to massive pulmonary embolism. Of the 167 patients undergoing modified radical mastectomy only one died. One died after simple excision of the tumour and three after insertion of radium needles. Two of these last five deaths were due to massive pulmonary embolism, and two were due to pulmonary infarction following repeated embolism. Of the nine deaths in the entire series seven were therefore due to thrombo-embolic complications, with five deaths due to massive embolism.

Morbidity.—In the course of the analysis the question of treatment morbidity was investigated, special attention being directed to the problem of the swollen arm, limitation of shoulder movement, radionecrosis, and brachial plexus palsy. The first of these complications was the one in which we were most interested, particularly in trying to determine what part extensive surgery and radiotherapy play in its production. The true incidence of some complications may well have been higher than the notes reveal, and the severity of such a complication as oedema cannot be accurately estimated. It is possible that some of the original observers may have been more punctilious in recording the complications after certain methods of treatment. Notwithstanding all these factors, we believe the information collected to be of value.

Oedema of the Arm.—Surgeons are shy to admit responsibility for this complication and the radiotherapist is often blamed. Some surgeons indeed claim that they rarely see this complication after surgery alone. In Table VIII is shown the incidence of oedema of the arm following different methods of treatment. The three different types of surgical procedure are listed irrespective of whether irradiation was also given, the proportion of irradiated cases being not greatly different in each group. There is no doubt about the significance of the lower incidence following simple surgery. In comparing the results for all methods of surgery alone with all methods plus irradiation the incidence of oedema of the arm is 12% in each group. A further factor of some importance in causing oedema of the arm is sepsis at the operation site; this was emphasized by Halsted (1921) many years ago. Table VIII also shows how the incidence of oedema of the arm was related to healing of the wound after radical or modified radical mastectomy. Oedema was twice as frequent in those cases developing haematoma, sepsis, or slough as those with uncomplicated healing.

TABLE VIII.—*Incidence of Post-operative Oedema*

	Total No. of Cases	Cases of Oedema	
		No.	%
All surgery	734	87	12
Simple surgery*	229	11	5
Radical surgery*	338	48	14
Modified radical surgery*	167	28	17
Surgery with irradiation	446	52	12
,, without ,,	288	35	12
Radical and modified radical surgery:*			
With primary healing	278	35	13
,, sepsis or sloughs	84	20	24
,, haematoma	65	13	20

* With or without irradiation.

There were 78 cases with no record of the healing of the radical wound.

Recurrences in the Treated Area

Among the whole series there were 297 (28%) for whom local recurrences were recorded; of these, 53% were in the first year, 74% within the first two years, and 91% within the first five years.

In analysing the incidence of local recurrences there are considerable difficulties. First there is the question of definition. We have not always found it possible to distinguish, from the records, between a tumour persisting after conservative treatment and a true local recurrence. In a retrospective inquiry there is clearly no way out of this difficulty. Then there is the problem of how to express the figures themselves. Smithers *et al.* (1952) recommend the use of the "recurrence-free rate," which is the percentage at any time who are alive and have suffered no local recurrence. This method does not, however, take into account the time of onset of the local recurrence, making no distinction, for instance, between two patients, both surviving for five years, one of whom has a recurrence in the first and the other in the fifth year.

Our somewhat tentative solution to this problem has been to devise a ten-year local recurrence index, which is defined as follows:

$$\text{Local recurrence index} = \left(1 - \frac{\text{Total completed recurrence-free years}}{\text{Total completed years of survival}}\right) \times 100$$

In calculating both these totals only the first ten years after treatment are taken into account; recurrence-free years are those between treatment and the onset of the first recorded local recurrence, irrespective of whether it was cured. An advantage of the index is that it is largely independent of the actual survival rate, and it is therefore possible to compare groups in which the proportions of the clinical stages are not the same.

Table IX shows the number of cases of local recurrence recorded after each form of treatment and also the local recurrence index. The high figures for *x*-ray and radium treatment are no doubt partly due to the confusion of persisting tumours with local recurrences. So far as the other methods are concerned, it will be seen that the lowest

TABLE IX.—*Local Recurrences in Stages I–III*

		No. of Cases	No. with Local Recurrence Within Ten Years	Ten-year Local Recurrence Index (%)
Simple surgery	Alone	55	20	16
	With *x* rays	63	27	14
	,, radium	98	29	13
Radical ,,	Alone	180	37	6
	With *x* rays	143	30	8
Modified radical surgery	Alone	45	15	15
	With *x* rays	48	10	9
	,, radium	67	14	15
X rays alone		71	19	24
Radium alone		137	64	31

This table excludes the untreated cases and the 6 cases treated with radical surgery and radium.

indices are for radical surgery, and that the addition of radiotherapy seems to have no appreciable effect.

All this is, however, somewhat speculative, and we should be unwilling to base any firm conclusions on these figures. The method is presented partly with the object of stimulating comment and criticism, for the subject is one that seems to have been neglected. Not only should consideration be given to the theoretical aspects of this problem, but, more important, a large series should be followed up with the specific aim of discovering the usual pattern of local recurrences and their effect on survival. We believe that, while the treatment of local recurrences may rid the patient of an obvious focus of disease, it may not in most cases be a means of prolonging life.

Discussion

The present series represents a group of cases treated long enough ago for us to be able to assess the long-term results. The fact that radiotherapy technique was neither so highly developed nor so widely accepted as at the present time suggests that the results obtained then should be bettered to-day.

The most impressive finding in this series is the remarkable similarity in survival rates following different methods of treatment. All the main treatment methods analysed seem to have been equally effective in stages I and II. It must, however, be frankly recognized that all methods of treatment may have been equally ineffective in prolonging life. While properly applied treatment has great palliative value it is important to ask to what extent treatment has affected survival. The only truly curable cases are those in which there is no distant spread at the time of the initial treatment, and complete eradication of the disease is probably not often achieved.

The advocacy of conservative surgery and radical radiotherapy by McWhirter (1948), although it has not yet met with universal approval, has encouraged many surgeons to take a much more critical view of their results. Some have been slow to appreciate the fact that the best results of radical surgery are due to selection of the most favourable cases, and it has not been easy for such people to accept a less radical doctrine. Great credit is due to McWhirter and the surgeons of the Edinburgh school, who have given the more reluctant amongst us the opportunity of watching a bold experiment. Even greater credit is, however, due to Geoffrey Keynes, who had the courage to adhere to a method of treatment which, 20 years ago, was regarded by most surgeons as totally inadequate.

The advocates of radical mastectomy, while conceding the point that a grossly diseased axilla is not benefited by dissection, believe that a real advantage accrues in those patients with minimal axillary gland involvement. But is this really so ? Is it not possible that axillary and internal mammary lymph node involvement are of equally serious significance, and that, despite the seeming accessibility of the former, in neither instance is the disease truly curable ? If this is in fact true, it may be the main reason why the results of simple surgery compare so favourably with those of the more radical procedure. The supporters of radical mastectomy may have attached too much importance to the removal of the axillary glands. Does their accessibility justify the assumption that their removal is advantageous to the patient ? The possible advantage of axillary dissection in those patients with low axillary gland involvement may be offset by the frequent occurrence of extensive axillary disease which even the most experienced surgeon may not detect before operation.

The definite morbidity of radical mastectomy, and the fact that it seems to offer no greater survival rate, suggest that the time has come to ask whether this operation has more than a limited place in the surgeon's armamentarium. The only possible advantage we have adduced in favour of the radical operation is the lower local recurrence index when compared with simple surgery. However, many of the local recurrences in the simple surgery group occurred in those cases treated by simple excision of the tumour ; and modern radiotherapy and simple mastectomy might show up more favourably in this respect. It might be expected that a method of treatment which gives a low local recurrence index would also show a better overall survival rate. It is, however, possible that local recurrence *per se* is an infrequent source of distant metastases and that the appearance of the latter has been determined quite independently of the former. No firm decision can be given on this matter, and the subject is worthy of further investigation.

In the absence of facilities for modern radiotherapy it may be that the radical operation, confined to the most favourable cases, offers the best chance of cure and of preventing local recurrence.

Although we doubt the value of the radical mastectomy operation it is noteworthy that some surgeons, and more especially in the United States of America, have advocated even more radical operations involving removal of costal cartilages and excision of the anterior mediastinal glands. In our opinion such operations are unjustifiable and may in many cases be positively harmful to the patient. Some of the recent interest in this over-radical surgery has been due to the too literal interpretation of Handley's work by the enthusiastic surgeon. The anterior mediastinal glands are readily accessible to irradiation, and it would seem more reasonable to treat them in this way rather than to remove them by block dissection.

So far as the results of radiotherapy are concerned we are reluctant to draw conclusions from our own material. Owing to variations in technique during the decade in question, it has not been easy to show that radiotherapy increased the survival rate or lowered the incidence of local recurrence, although there are some indications that this was so. A carefully planned research would be necessary to elucidate this matter.

To determine a treatment policy suited to each individual type of case, although perhaps an ideal, is a difficult problem. Points about the case which are readily recognized after operation, and detailed examination of the pathological specimens, are not easily appreciated beforehand. To practise several variations in treatment is not always so easy or so logical as it seems. There are so many unknown factors to be taken into consideration that in these circumstances, and in the present state of our knowledge, a great deal can be said for simple mastectomy and radical irradiation in the majority of cases. Simple excision of the tumour and radiotherapy is a reasonable alternative in many elderly patients, and in some of those with small tumours. The great importance of the most careful clinical examination, supplemented by the necessary diagnostic *x*-ray investigation, should be continually emphasized as the only way to avoid unnecessary treatment for the patient with distant disease.

Summary

The purpose of the paper is to present an analysis of the results obtained in 1,044 cases of carcinoma of the female breast first seen at St. Bartholomew's Hospital during 1930–9.

Follow-up of all but 30 untraced patients was complete until May, 1951, enabling 10-year survival rates to be calculated for the whole series and 15-year rates for cases registered in 1930–5.

The distribution by clinical stages was as follows : I, 32.5% ; II, 28.9% ; III, 27.4% ; IV, 10.2% ; unstaged, 1.1%. Distribution by age and site of tumour was similar to that given in other published series.

Differences in clinical staging are not explicable only in terms of delay in seeking advice. Of cases with more than two years' history 31% were still in stage I, whilst 19% of those with a history of one month or less were in stages III and IV.

Pathological investigation of cases with axillary dissection revealed that the clinical assessment of the glands was wrong in 29% of stage I cases and 23% of stage II

cases. There was no clear association between length of history and gland involvement.

The various methods of treatment are discussed. Simple surgery was undertaken in 229 cases, more than half of which were treated by simple excision of the tumour. Radical mastectomy was done in 338 cases, and the modified radical operation in 167. Radium treatment without surgery was used in 149 cases, and *x* rays alone in 114. Forty-seven cases were not treated. Of the cases treated surgically, about two-thirds were also given irradiation. This type of treatment became more frequent towards the end of the period, and at the same time *x* rays tended to replace radium, particularly in combination with simple surgery.

Five- and ten-year survival rates, adjusted for variations in age distribution, are calculated for different clinical stages and treatment groups. The adjusted rates for all treated cases in stage I were as follows: five-year, 72%; ten-year, 51%. The corresponding figures for stage II were: 39% and 26%. The rates for the individual treatment groups showed no appreciable departure from these figures despite the fact that simple surgery consisted merely of local excision in more than half the cases; nor did the addition of irradiation affect the rates, although it is possible that selection of cases may have concealed some of the benefits of radiotherapy.

Attention is drawn to the lower survival rates in the cases assessed clinically to be in stage II but with axillary glands pathologically free, compared with stage I cases with glands involved.

The mortality of radical mastectomy was 1.2%. Oedema of the arm occurred after radical surgery in 14% of cases, compared with 5% after simple surgery, and was almost twice as frequent when the radical wound gave rise to complications as in those with primary healing.

There seemed to be fewer local recurrences following radical surgery than other types of surgery, but the addition of radiotherapy appeared to make no difference in this respect.

It was concluded from a general discussion that where efficient radiotherapy is available radical mastectomy should be abandoned in favour of conservative surgery.

We wish to express our gratitude to Mr. Reginald Vick, Mr. Geoffrey Keynes, Sir James Paterson Ross, and the other members of the staff of St. Bartholomew's Hospital who allowed us to undertake a study of patients who were under their care. Our thanks are also due to Dr. Christine Abernethy and Mrs. Perkins, who have both contributed to the completeness of the follow-up records, and to the staffs of the follow-up and statistics departments, on whom fell much of the routine work.

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TREATMENT BY OESTROGENS OF PULMONARY METASTASES FROM BREAST CANCER

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In a previous paper, based on treatment of 152 cases of advanced breast carcinoma by oestrogens, one of us has commented on the encouraging results in cases of pulmonary metastasis. It was recorded that out of 25 cases of pleural or lung metastases treated by oestrogens there were nine survivals for longer than 12 months (Stoll, 1950). In the majority of these cases, also, there was radiological evidence of regression of these metastases. This achievement is remarkable in view of the average survival of only about three months in similar untreated cases. The series has now been expanded to 61 cases treated at the London Hospital Radiotherapy Department between 1943 and 1950. In addition, the results are compared with a series of 66 cases of pleural and lung metastases seen during the same period but not treated by oestrogens. All cases were supervised by one or other of us.

The background of the cases must first be examined. The number of cases of breast carcinoma recorded with pleural or lung metastases from 1943 to 1950 was 159, and the number of cases with pleural or lung metastases, verified radiographically, was 127. Of these latter cases, oestrogens were prescribed in 61 and not prescribed in 66. The selection of cases for hormone administration was statistically random but not controlled. When the cases came to be analysed it was found that the proportion of cases of a younger age group was considerably higher in the untreated than in the treated group (Table VI). That this distribution did not influence the results is seen in the same table, where for each group the age of the patient was found to exert no influence on the length of survival. This fact is further commented on later.

Length of Survival after Oestrogen Treatment of Pulmonary Metastases

TABLE I.—*Months of Survival in Treated and Untreated Cases*

Months Survival	Cases of Pleural Metastasis		Cases of Lung Metastasis		Total	
	T.	U.	T.	U.	Treated	Untreated
1–3	17	31	6	12	23 (5 still alive)	43 (all dead)
4–6	9	10	3	4	12 (4 ,, ,,)	14 (,, ,,)
7–11	5	3	2	1	7 (2 ,, ,,)	4 (,, ,,)
12+	9	4	10	1	19 (9 ,, ,,)	5 (,, ,,)
Total ..	40	48	21	18	61	66

TABLE II.—*Comparative Percentage Survival in Treated and Untreated Cases*

	Treated Group	Untreated Group
Died within 3 months ..	29·5%	65%
,, 4–11 months	21·5%	27·5%
Survival over 12 months ..	31%	7·5%
Still alive, 1–11 months ..	18%	—
	100%	100%